



CDB SEMINAR

Speaker:

Kevin A. Roth

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Title:

“Bcl-2 and Caspase Regulation of Neuronal Death and Degeneration – Lessons from Gene-Disrupted Mice.”

Date:	Tuesday, August 24
Time:	16:00 P.M. ~ 17:00 P.M.
Place:	1F Auditorium of Building C, CDB

Summary:

Neuronal apoptosis occurs during normal mammalian nervous system development and in a variety of neuropathological processes including hypoxic-ischemic injury, neurodegenerative diseases, and fetal alcohol syndrome. We have used mice with targeted gene disruptions in specific bcl-2 and caspase family members, in combination with a variety of in vivo and in vitro models of neuronal cell death, to define the cell- and stimulus-specific molecular pathways of death. During embryonic nervous system development, programmed cell death proceeds in three cellular phases. The first involves neural precursor cells and is critically regulated by caspase-9 and caspase-3 activation. The second occurs in immature neurons and is largely regulated by Bax and Bcl-XL expression. The third phase occurs in synapse bearing neurons and involves various Bcl-2 family members including Bcl-2, Bcl-XL and Bax but is largely independent of caspase activation. In contrast with the clear role of Bcl-2 and caspase family members in naturally-occurring neuronal cell death, involvement of these molecules in pathological cell death depends significantly on the neurodegenerative insult and the maturation state of the brain. For example, Bax deficiency produces virtually complete inhibition of Bcl-XL deficiency-induced immature neuron death in the embryonic nervous system and from ethanol-induced neuron death in the neonatal mouse brain. Bax deficiency however, does not provide protection from the neuron death promoting effects of cathepsin-D deficiency or from synapse loss and neurological symptoms in a transgenic mouse model of familial prion protein disease. These studies are important for defining the regulation of neuron death during health and disease.

Host: Hideki Enomoto <Neuronal Differentiation and Regeneration, CDB>

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